Preliminary results : effect of p38α MAPK inhibitor on neuroinflammation assessed by DPA-714 in early Alzheimer disease.

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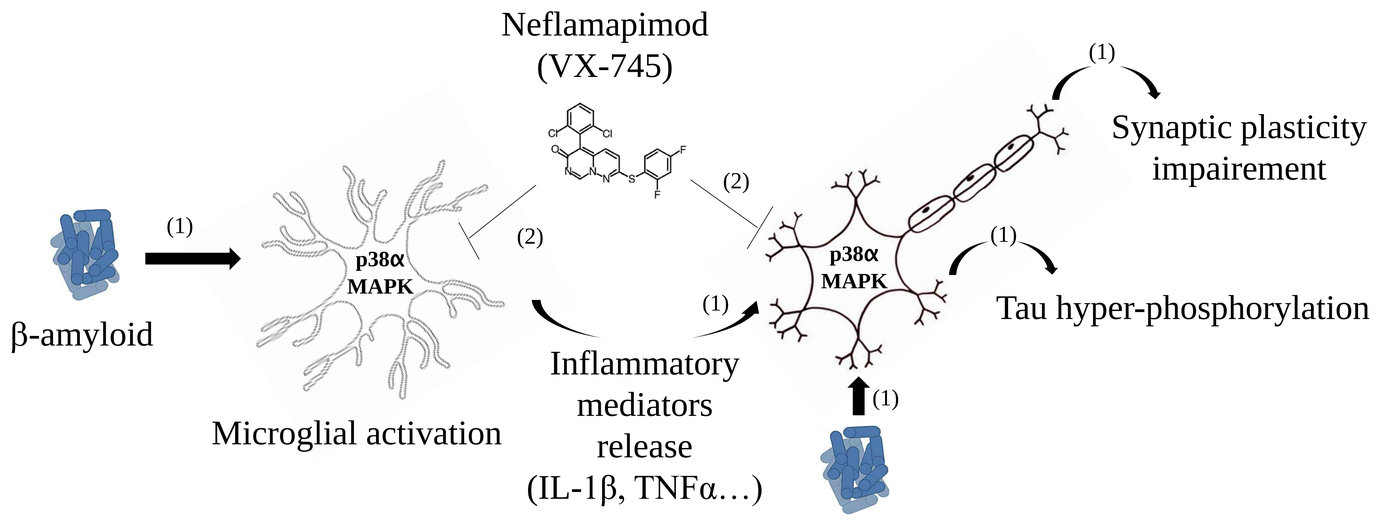
Background and objectives



The V.I.P. project

A proof of concept study to evaluate the efficacy of **V**X-745 (Neflamapimod) on brain **I**nflammation using DPA-714 in **P**ET scan on selected Alzheimer disease patients.

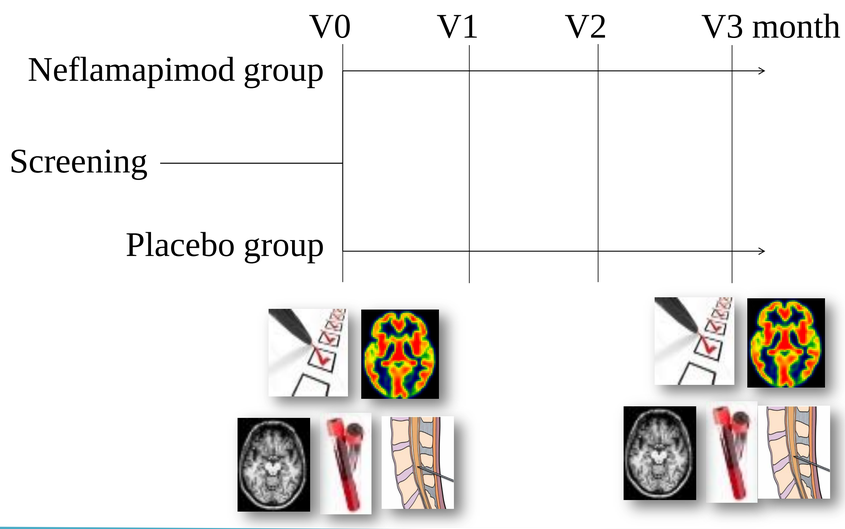
Objectives :
1) Compare the intensity of neuroinflammation using DPA714 PET scan between treated and placebo groups after 12 weeks of treatment.
2) Assess the effect of Neflamapimod on the neuropsychological state, brain structure and inflammation biomarkers.

Design of the study

N = 40 AD patients at a prodromal stage [3]

➡ Inclusive :
_Objective memory imparement
_Documented amyloïdopathy using CSF [4]
_MMSE >20

➡ Exclusive :
_Any neurodegenerative disease other than AD
_Any incompatible psychatric disorders
_Any history of inflammatory chronic events



Preliminary results

Patient	Gender	Age (years)	Education (years)	APOE polymorphism	MMSE score at screening	Biomarkers profiles [5] at screening
001	⚧	61	12	E3/E4	30/30	A+T+(N)+
002	⚧	66	11	E2/E4	30/30	A+T+(N)+
003	♂	80	12	E3/E3	27/30	A+T+(N)+
004	⚧	60	12	E3/E4	24/30	A+T+(N)+
005	♂	64	12	E3/E3	24/30	A+T+(N)+
006	♂	81	9	E3/E3	28/30	A-T+(N)+
007	⚧	76	11	E3/E4	24/30	A+T+(N)+
008	♂	64	12	E4/E4	22/30	A+T+(N)+
009	♂	64	12	E3/E4	24/30	A+T+(N)+
010	♂	75	12	E4/E4	24/30	A+T+(N)+

Figure 1 : demographic results

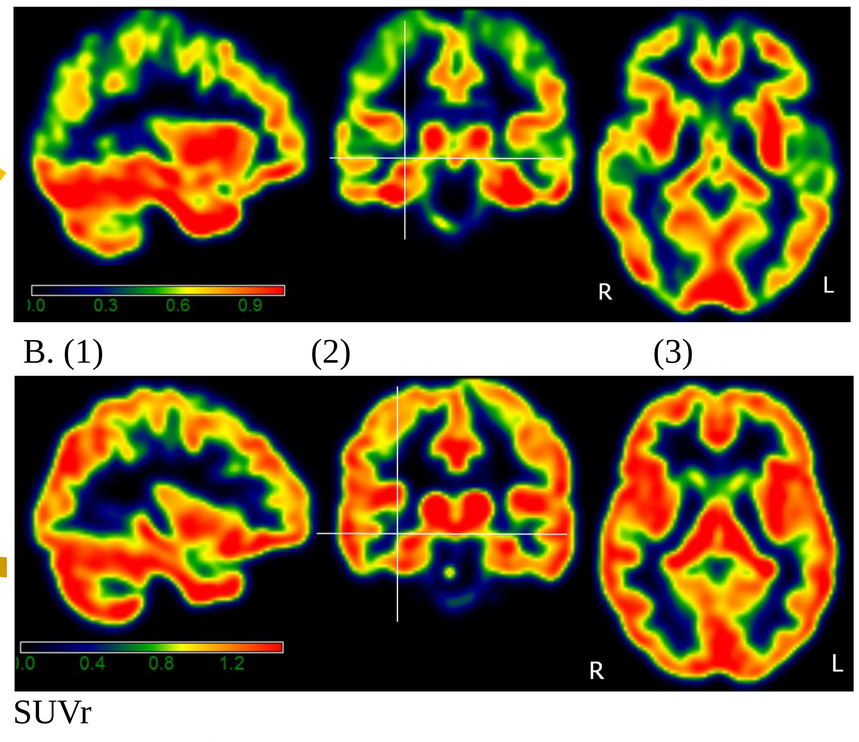


Figure 2 : PET scan [^{18}F] DPA-714 of (A) an hypothetical placebo group subject (B) an hypothetical neflamapimod group subject, (1) in sagittal, (2) frontal, (3) axial view. The cerebellar grey matter was selected as pseudo-reference region [6]. TSPO polymorphism was not taken into account.

References : (1) Corea and Eales, 2012 ; (2) Alam, 2015 ; Alam et al., 2017 ; (3) Dubois et al., 2014 ; (4) Mattsson et al., 2009 ; (5) Jack et al., 2018 ; (6) Lyoo et al., 2015.